UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/680,471	10/06/2000	Lorenzo Williams	0459-0490P	8775

2292 7590 06/12/2003

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
GAKH, YELENA G

ART UNIT	PAPER NUMBER
1743	13

DATE MAILED: 06/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

A-S-13

Office Action Summary	Application N .	Applicant(s)	
	09/680,471	WILLIAMS, LORENZO	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1743	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-30,32,34-38,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-30,32,34-38,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Amendment filed on 04/24/03, is acknowledged. Claims 33 and 39 are cancelled. Claims 1-2, 5-30, 32, 34-38 and 40-41 are pending in the Application.

Response to Amendment

2. The rejection of claim 39 under 35 U.S.C. 112, second paragraph is withdrawn since the claim is cancelled.

3. The pending claims remain rejected over the prior art on the same grounds that were established in the previous Office action.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. **Claims 1-2, 5-12, 15-30 and 33-36** are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta et al. (US 6,306,590 B1) in view of Frank (IDS).

Mehta discloses microfluidic matrix localization apparatus and method for "**screening**, manipulating and assessing fluidic reagents, reagent mixtures, reaction products (including the products of DNA sequencing reaction) and the like. The invention provides integrated systems for performing a variety of chemical, biochemical and biological experiments and other fluidic operation, including PCR, DNA sequencing, **integrated or sequential screening of chemical or biological libraries**, and the like" (col. 5, lines 25-34). The invention is based on a surprising discovery "that the PCR reaction can be performed in the presence of a variety of sieving matrices, including: agarose, linear polyacrylamide, methyl-cellulose, polyethylene oxide and hydroxy ethyl cellulose and that resulting PCR products are separated in the microfluidic devices" (col. 4, lines 40-45). "In preferred embodiments, the components of the PCR reaction mixture are mixed with the sieving matrix in a microfluidic channel, e.g., a channel on a LABCHIP™. The apparatus can include one or more additional channels crossing the microfluidic channel and optionally includes fluid (or joule heating) means such as an electrokinetic controller. Detection regions in the channels, and corresponding detectors are also useful. The PCR products are typically **electrophoresed** through the channels to achieve product separation. It will be appreciated that separations chips comprising **a single matrix separations phase** are produced as described above, thus, **for this embodiment, multiple fluidic phases in the apparatus are not necessary**. However, additional fluidic phases can be placed in additional channels or channel regions in fluid communication with a channel region comprising the PCR sieving mixture for electrophoretic or electroosmotic movement of the PCR components or products in the chips. For example, in some aspects a PCR reaction product is selected for further manipulations such as cloning, sequencing or the like, all of which are performed in PCR chips (see also, USSN 60/068,311, entitled "Closed Loop Biochemical Analyzer" by Knapp, filed Dec. 19, 1997 and U.S. Pat. No. 6,235,471" (col. 17, lines 29-52).

Thus, the PCR products are prepared in a bulk of a stationary phase (a mix with the sieving matrix) and separated in the same bulk, with optional addition of detection regions in the channels (screening of the compounds).

Mehta further teaches that the substrates of the microfluidic devices are made of glass, quartz, silicon, polymers, (col. 6, lines 5-10), as well as silica gels (col. 9, lines 45-65) and activated aluminas (col. 10, lines 3-14), and that they may optionally include a planar element

which overlays the channeled portion of the substrate, enclosing and fluidly sealing the various channels, wells and other microfluidic elements (col. 6, lines 35-40). The devices "are from about 0.01 to about 0.1 cm thick" (col. 6, lines 52-53). Mehta mentions such analytical (screening) techniques as "autoradiography, spectroscopy, microscopy, photography, mass spectrometry, nuclear magnetic resonance and many other techniques for observing and recording the results of mixing reagent", as well known methods of screening of the reaction products (col. 1, lines 5-15).

Mehta does not specifically disclose screening of the separated products in the same bulk stationary phase by **biological or biochemical methods**.

Frank discloses a method for preparing and screening a plurality of compounds on a matrix support by synthesizing a library of compounds on a stationary phase and screening them by biological or biochemical methods, as described in section "Antibody Binding Assay" (p. 9224).

It would have been obvious for anyone of ordinary skills in the art to apply a specific screening step, involving biological or biochemical methods, disclosed by Frank, in Mehta's method, because Mehta indicates a screening step as a part of her invention involving biologically important compounds, and Frank demonstrates the efficiency and straight-forwardness of the method of synthesis and **biological or biochemical** screening of libraries of biologically important compounds directly on the same substrate.

Although Mehta in view of Frank do not specifically disclose a TLC plate, it would have been obvious for anyone of ordinary skills in the art to perform synthesis, separation of the products and their screening on the TLC plate, because Mehta's synthesis is directed toward PCR products, which are conventionally separated by electrophoresis, and which therefore requires applying electrical field and the chip setting, while the separation of many other products can be conducted by simple TLC, and which therefore can be performed on much simpler and cheaper TLC plate.

It would have been obvious for anyone of ordinary skill in the art to use any of the liquid phase mixtures recited in claim 28, because choosing the solvent mixture for developing TLC plate is a routine procedure in analytical chemistry.

7. **Claims 13-14** are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta in view of Frank, as applied to claims 1-2, 5-12, 15-30 and 33-36 above, and further in view of Hudak (US 6,034,361).

Although Mehta discloses "thermocycling in microscale devices, including thermocycling by joule heating", Mehta in view of Frank do not teach microwave-assisted synthesis.

Hudak emphasizes in the Background of the Invention, that using microwave heating to promote the progress of one or more sample preparation steps or chemical synthesis steps is well known in the art (col.1, lines 14-16).

It would have been obvious for anyone of ordinary skill to use microwave radiation to provide "joule heating" in Mehta-Frank's method, because Mehta teaches necessity of "joule heating" for PCR, and Hudak demonstrates an easy way to provide it with microwave radiation. It would have been obvious to place the bulk of the stationary phase with the reagents into a microwave cave to provide such heating.

8. **Claims 37-38** are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta in view of Frank, as applied to claims 1-2, 5-12, 15-30 and 33-36 above, and further in view of Bataillard (US 5,482,372) or Brocklehurst et al. (US 5,739,003).

Mehta in view of Frank do not specifically disclose detection of biological effects of a compound interacting with a microorganism or enzyme as a screening step.

Bataillard mentions "enzymatic assays and drug screening using microorganisms" (col. 2, lines 38-40); Brocklehurst emphasizes that "drugs, e.g. antibiotics, must be screened for activity against particular microorganisms and the concentration required for achieving that effect must be determined" (col. 1, lines 32-35).

It would have been obvious to modify Mehta-Frank's method specifically for creating and screening drug libraries by using microorganisms in the screening step, because such step is standard in screening drugs, as disclosed by Bataillard or Brocklehurst.

9. **Claims 40 and 41** are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta in view of Frank, as applied to claims 1-2, 5-12, 15-30 and 33-36 above, and further in view of the well-known prior art discussed by Wolfbeis (DE 3,701,833 A1).

Mehta in view of Frank do not particularly disclose detection of catalytic activity produced by observed changes in absorption of light or detection of fluorescence due to a cleaved substrate.

Wolfbeis mentions "known methods for the optical determination of the catalytic enzyme activity of a sample, which use enzyme substrates which are cleaved under the influence of the enzyme to be measured and decompose to colored or fluorescent products, where the increase in color or fluorescence intensity per unit time is regarded as a measure of the enzymatic activity" (Abstract).

It would have been obvious for anyone of ordinary skills in the art to conduct spectroscopic analysis of the substrate in order to determine the enzymatic (catalytic) activity of the compounds, as disclosed in the prior art discussed by Wolfbeis, in modified Mehta-Frank's bulk stationary phase, because this is a conventional way for determining enzymatic activity of the compounds, which can be readily obtained by modified Mehta-Frank's method.

Response to Arguments

10. Applicant's arguments filed 04/24/03 have been fully considered but they are not persuasive. First of all, the examiner cannot agree with the statement of the Applicant that Mehta does not provide a disclosure for a "bulk of a stationary phase". As it was particularly pointed out by the examiner, Mehta specifically discloses such bulk stationary phase: "it will be appreciated that separations chips comprising *a single matrix separation phase* are produced as described above, thus, *for this embodiment, multiple fluidic phases in the apparatus are not necessary*" (col. 17, lines 39-42). It is not clear, what is the difference between Metha's "single matrix separation phase" and "a bulk stationary phase" of the instant invention, as they comprise the same material and are used exactly for the same purpose of performing reactions, separation and screening of plurality of products in the same phase? Further, the Applicant states that according to Mehta, conducting the plurality of reactions requires the "multiplicity of multiphasic compartments". The examiner would appreciate if the Applicant could indicate where specifically in the disclosure Mehta gives such statement, as she failed to find it.

Regarding the combination of Mehta and Frank references. Mehta specifically indicates that "present invention provides apparatus, systems and methods for dramatically increasing the speed and simplicity of **screening**, manipulating and assessing fluidic reagents, reagent mixtures, reaction products (including the products of DNA sequencing reactions) and the like. The invention provides integrated systems for performing a variety of chemical, **biochemical and biological experiments** and other fluidic operations, including PCR, DNA sequencing, integrated or sequential screening of chemical or biological libraries, and the like" (col. 5, lines 25-35), which may involve biochemical and biological method of screening. Mehta does not in particular disclose biological or biochemical screening methods. Frank teaches exactly such biological or biochemical screening methods for bioorganic compounds obtained by spot synthesis on the substrate. It is completely unclear, why Frank teaches away from using his screening step involving biological or bio-chemical methods in Mehta's method, when both inventions deal with screening of separated compounds on the substrate? The fact that Frank and Mehta had different approaches to separation of the compounds on the substrate has nothing to do with the screening step. Since the screening step is not related to the way in which separation of the biologically important compounds on the substrate is achieved, Frank cannot teach away from using his screening step in Mehta's method. Moreover, using Frank's biological screening techniques is an obvious modification of Mehta's method, comprising such screening step, especially since she mentions "performing a variety of chemical, biochemical and biological experiments" on the substrate.

The Applicant did not provide any further arguments regarding rejections of dependent claims based on other references.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (703) 306-5906. The examiner can normally be reached on 10:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

YG
June 6, 2003

Jill Warden
Supervisory Patent Examiner
Technology Center 1700